EPA/EPO/OEB
D-80298 München
+49 89 2399-0
TX 523 656 epmu d
FAX +49 89 2399-4465

Europäisches Patentamt | European Patent Office | Office européen des brevets

Generaldirektion 2 | Directorate General 2 | Direction Générale 2

Telephone numbers:
Primary Examiner (substantive examination) +49 89 2399-7197
Formalities Officer / Assistant (Formalities and other matters) +49 89 2399-8062

Stuttard, Garry Philip
Urquhart-Dykes & Lord
Tower North Central
Merrion Way
Leeds LS2 8PA
ROYAUME-UNI

RECEIVED
27 FEB 2004
DL LEEDS

Application No. 01 942 558.6 - 2406	Ref. GS/AMW/P207142	Date 24.02.2004
Applicant Diatranz Limited		

Communication pursuant to Article 96(2) EPC

The examination of the above-identified application has revealed that it does not meet the requirements of the European Patent Convention for the reasons enclosed herewith. If the deficiencies indicated are not rectified the application may be refused pursuant to Article 97(1) EPC.

You are invited to file your observations and insofar as the deficiencies are such as to be rectifiable, to correct the indicated deficiencies within a period

of 4 months

from the notification of this communication, this period being computed in accordance with Rules 78(2) and 83(2) and (4) EPC.

One set of amendments to the description, claims and drawings is to be filed within the said period on separate sheets (Rule 86(1) EPC).

Failure to comply with this invitation in due time will result in the application being deemed to be withdrawn (Article 96(3) EPC).

SOMMERFELD T M
Primary Examiner
for the Examining Division

Enclosure(s): 4 page/s reasons (Form 2906)

Registered Letter
EPO Form 2001 07.02CSX

Bescheid/Protokoll (Anlage) | Communication/Minutes (Annex) | Notification/Procès-verbal (Annexe)

Datum / Date / Date: 24.02.2004 | Blatt / Sheet / Feuille: 1 | Anmelde-Nr.: / Application No.: / Demande n°: 01 942 558.6

The examination is being carried out on the **following application documents:**

Text for the Contracting States:
AT BE CH LI CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR

Description, pages:
1-24 as published

Claims, No.:
1-42 as received on 27.08.2001

Drawings, sheets:
1/4-4/4 as published

The following documents mentioned in the search report are cited in this communication:

D1: WO 96 40178 A (RES CORP TECHNOLOGIES INC) 19 December 1996 (1996-12-19)

D2: CALAFIORE RICCARDO: 'Actual perspectives in biohydrid artificial pancreas for the therapy of type 1, insulin-dependent diabetes mellitus.' DIABETES METABOLISM REVIEWS, vol. 14, no. 4, December 1998 (1998-12), pages 315-324, XP009007646 ISSN: 0742-4221

D3: US-A-5 888 705 (OTONKOSKI TIMO PYRY JUHANI ET AL) 30 March 1999 (1999-03-30)

D4: BRANDHORST HEIDE ET AL: 'Significant progress in porcine islet mass isolation utilizing Liberase HI for enzymatic low-temperature pancreas digestion.' TRANSPLANTATION (BALTIMORE), vol. 68, no. 3, 15 August 1999 (1999-08-15), pages 355-361, XP009008045 ISSN: 0041-1337

D5: CA-A-2 216 055 (ROSENBERG ET AL., MCGILL UNIV. CA) 19 March 1999 (1999-03-19)

D6: CAVANAGH T J ET AL: 'Improved pig islet yield and post-culture recovery using liberase PI purified enzyme blend.' TRANSPLANTATION PROCEEDINGS, vol. 30, no. 2, March 1998 (1998-03), page 367 XP002235318 Sixth Congress of the International Pancreas and Islet Transplant Association;Milan, Italy; September 24-27, 1997 ISSN: 0041-1345

D7: BASTA G ET AL: 'Xenotransplantation of microencapsulated neonatal porcine islets (NPI) in diabetic recipients: Pre-clinical trials.' ACTA DIABETOLOGICA, vol. 37, no. 3, September 2000 (2000-09), page 145 XP001146450 20th Workshop of the Study Group on Artificial Insulin Delivery, Pancreas and Islet Transplantation;Igls, Austria; January 28-30, 2001 ISSN: 0940-5429

D9: NZ-A-250834 ✓

D10: 'Transplantation of pancreatic islets contained in minimal volume microcapsules in diabetic high mammalians','RICCARDO CALAFIORE ET AL.','ANNALS OF THE NEW YORK ACADEMY OF SCIENCES',',875//00-00-1999,219-232,✓

D11: SUN YI-LU et al. "Normalisation of diabetes in spontaneous diabetic cynomologus monkeys by xenografts of microencapsulated porcine islets without immunosuppression" JOURNAL OF CLINICAL INVESTIGATION, vol. 98, No. 6, 1996 p.1417-1422 ✓

D13: SUN YI-LU et al. "Porcine pancreatic islets: isolation, micorencapsulation and

xenotransplantation" ARTIFICIAL ORGANS, vol. 17 No. 8, 1993, p.727-733

D14: WEBER C J et al. "Evaluation of graft-host response for various tissue sources and animal models" ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, vol. 875, 1999, p.239-254

D15: AU-A-81864/98 ✓

1. Introduction

1.1. The present application discloses methods for xenotransplantation of neonatal porcine pancreatic beta islets into diabetic mammalians.

1.2. An international preliminary examination report has already been drawn up for the present application in accordance with the PCT. The deficiencies mentioned in that report have been taken into account.

2. Amendments (Art. 123(2) EPC)

Claim 15 appears not to have support in the application as filed and is thus not allowable under Art. 123(2) EPC. Indeed, while support could be found in the specification for "antibiotic" and "ciproxin", no reference to "quinaline antibiotic" was found. This amendment thus appears to be both an unallowable selection from the general concept of antibiotic and a generalization from the single antibiotic ciproxin.

If in disagreement the Applicants are requested to indicate the basis on the originally filed application for this amendment.

3. Priority (Art. 87 EPC)

The present application claims priority from 12 documents. At least the priority document filed on 15.08.00 appears to disclose the relevant subject-matter of the application. This priority is considered valid (Art. 87 EPC) and the P,X document of the search report (document D7), which was published after this priority date, is not citable as prior art.

4. Novelty and inventive step (Arts. 54(2) and 56 EPC)

4.1. Claim 1 is directed to a method of preparing xenotransplantable porcine islets, wherein pancreas of piglets from -20 to +10 days full term gestation are harvested, islets are extracted and exposed to nicotinamide either before or after harvesting or extracting.
All these technical features are contained in prior art documents D9 (e.g. claims 2 and 5) and D15 (e.g. claim 1).
Claim 1 is thus not novel (Art. 54(2)EPC). The same applies to claim 2.

4.2. Claims 3-16 merely specify further technical features that, if at all novel, cannot contribute for inventive step as they appear to be mere technical variations well known from the prior art: Liberase® is also used for pancreatic islet extraction in documents D4 and D6; human serum albumin is used in the culture medium of pancreatic islets in D3 (column 4 last paragraph especially last line; column 6 lines 37-41); IGF-1 is disclosed as promoting survival of islets cells in D5 and is used in the incubation medium in D1 (Example 8, page 70 lines 24-28); ciprofloxacin (another designation for ciproxin) is also used in the incubation medium in D4 (page 357 left column line 12).
Claims 3-10, 15 and 16 thus lack an inventive step (Art. 56 EPC).

4.3. Claims 17 to 28 and 31 add to the method of claim 1 the step of encapsulating the islets cells with a biocompatible xenotransplantable material which comprises an alginate. Also all the technical features of these claims were known from the prior art, namely: sodium alginate complexed with poly-L-ornithine is used in D2 (page 222 lines 13-15); double-wall outer membrane is disclosed in D14 (page 239 lines 23-29); capsules with diameters of 350 microns (D10: page 222 lines 9-10), 0.25-0.35 mm (D11: page 1418 left column lines 10-11; D13: page 728 right column lines 4-5) are also disclosed.
The further features of claims 29 and 30, which merely refer to the number of islets present in each capsule, do not appear to contribute for inventive step.
Claims 17-31 thus also lack an inventive step (Art. 56 EPC).

4.4. Claims 32-42 refer to the use of pancreatic beta islets cells for the transplantation of diabetic patients. All features listed seemed to be standard for the procedure

according to the prior art documents. Note that it is not even apparent from these claims that the islets to be transplanted should originate from piglets and should be prepared according to the method claimed in the preceding claims. Note furthermore that the use of a "trauma protecting agent" which is an anaesthetic (claims 32-33) is clearly standard in any transplantation procedure. Claims 32 and 33 are thus not novel (Art. 54(2)EPC); further claims 34-42, if novel, lack an inventive step (Art. 56 EPC).

5. Unity of invention (Art. 82, Rule 30 EPC)

For the sake of completeness, the present set of claims is also objected as lacking unity (Art. 82, Rule 30 EPC), since the special technical feature linking the present inventions is merely transplantation of pancreatic islets cells for treatment of diabetes, which was well known in the prior art (e.g. D1, D2, D9-D11, D13).

Thus at least the following two groups of inventions can be identified:

1- method of preparing xenotransplantable porcine islets with given technical steps (claims 1-31);

2- use of pancreatic beta islets cells (prepared by any method from any animal) for transplantation of diabetic patients (claims 32-42).

6. Conclusion

It is not at present apparent which part of the application could serve as a basis for a new, allowable claim. Should the applicant nevertheless regard some particular matter as patentable, an independent claim should be filed taking account of Rule 29(1) EPC. The applicant should also indicate in the letter of reply the difference of the subject-matter of the new claim vis-à-vis the state of the art and the significance thereof.